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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FALK, ANNE MARIE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 10/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/464,795	**Applicant(s)** ZHANG ET AL.	
	Examiner Anne-Marie Falk, Ph.D.	**Art Unit** 1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08 September 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *4* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *See Continuation Sheet*. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *38, 40, 41, 43, 45, 46, 49, 65-68, and 80*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER

Anne-Marie Falk, Ph.D.
Primary Examiner
Art Unit: 1632

Continuation Sheet (PTOL-303)

Continuation of 3. NOTE: The proposed claim amendments, if entered, would require new grounds of rejection. For example, Claims 38, 40, 41, 45, 46, 49, and 65-68 would be rejected under 35 U.S.C. 112, second paragraph, for indefiniteness for recitation of "said second control element" (Claim 38, line 9), because the term lacks antecedent basis. Moreover, the newly added limitation to "promoter" would require further consideration.

Continuation of 11. The request for reconsideration has been considered but does NOT place the application in condition for allowance because:

See above. Applicants' arguments have been fully considered, but do not overcome the standing grounds of rejection.

At page 6 of the response, Applicants assert that the amendment to recite the term "promoter" instead of "control element" fully addresses the utility rejection because "[i]t is abundantly plain to the skilled artisan that a promoter represents native gene expression. No support is offered for this assertion. The term "promoter" covers minimal promoters, truncated promoters, and promoters lacking their endogenous inducible elements. Thus, the presence of a "promoter" as broadly defined, would not represent native gene expression.

At page 6 of the response, Applicants assert that the Office has improperly construed the claims because "[t]he specification clearly and unambiguously defines the term 'control elements derived from a stress-inducible gene' to encompass only control elements that regulate transcription of at least one stress-inducible gene(s)." Not true. The express teachings with regard to the term "control elements" were acknowledged at pages 3-4 of the prior Office Action (final rejection, mailed 5/17/05) and are reiterated hereinbelow, and the term simply does not "encompass only control elements that **regulate transcription**" (emphasis added) as Applicants now assert.

With regard to the control element recited in the claims, the specification discloses the following at page 33:

> "The control element (e.g., a promoter) may be from the same species as the transgenic animal (e.g., mouse promoter used in construct to make transgenic mouse), from a different species (e.g., human promoter used in construct to make transgenic mouse), or a mixed control element (e.g., some control elements from a mouse promoter combined with some control elements of a human promoter)." Specification at page 33, lines 26-30.

The specification further discloses, at pages 11-12, that the "control element derived from a ... stress-inducible gene" may be as follows:

> "Typical control elements or expression control elements or regulatory sequences, include, but are not limited to transcription promoters, transcription enhancer elements, transcription termination signals, polyadenylation sequences (located 3' to the translation stop codon), sequences for optimization of initiation of translation (located 5' to the coding sequence), translation enhancing sequences, and translation termination sequences. Transcription promoters can include inducible promoters (where expression of a polynucleotide sequence operably linked to the promoter is induced by an analyte, cofactor, regulatory protein, etc.), repressible promoters (where expression of a polynucleotide sequence operably linked to the promoter is induced by an analyte, cofactor, regulatory protein, etc.), and constitutive promoters.
>
> Expression enhancing sequences typically refer to control elements that improve transcription or translation of a polynucleotide relative to the expression level in the absence of such control elements (for example, promoters, promoter enhancers, enhancer elements, and translational enhancers (e.g., Shine and Delagarno [sic] sequences))." Specification at pages 11-12.

Thus, in view of the specification's own definition the term "control element" does **not** "encompass only control elements that **regulate transcription**" (emphasis added) as Applicants now assert. As a first example, "sequences for optimization of initiation of translation" **do not regulate transcription.** As a second example, "translation enhancing sequences" **do not regulate transcription.** As a third example, "translation termination sequences" **do not regulate transcription.** Thus, Applicants' arguments are quite contrary to the teachings of the specification.

At page 6 of the response, Applicants state that "[i]nterestingly, the Examiner acknowledges later in the Office Action that the claims are not so broad as to cover control elements unrelated to stress-

related genes." This appears to imply that the Examiner suggested the contrary position elsewhere in the Office Action. Such is not the case. Applicants appear to be confusing promoters with control elements. They are not equivalent. As stated in the prior Office Action, the claims cover the use of expression cassettes **having any promoter at all.** The claims do not recite promoters, only control elements. The mere presence of a polyadenylation signal "derived from a first stress-inducible gene" and another identical polyadenylation signal "derived from a second stress-inducible gene" would be sufficient to meet the claim limitations (Claim 38) and would be induced by **nothing**. See the specification at page 11, lines 24-26 which states that "[t]ypical control elements ... include ... polyadenylation sequences." The promoter can be any promoter at all. **There is nothing in the claim that limits the promoter (or even requires a promoter).** The promoter, if one is even present, is not required to be derived from a stress-inducible gene. Applicants arguments are far afield from that which is claimed.

The remaining arguments are directed to the claims as amended, but the proposed claim amendments have not been entered for the reasons noted above and therefore the arguments are moot.

Applicants' arguments with regard to enablement, at pages 11-12 of the response, are identical to those presented at pages 7-9 of the reponse filed 2/18/05. These arguments have already been considered and addressed and are not found persuasive for the reasons set forth at pages 7-10 of the Office Action mailed 5/17/05.

The proposed amendment has not been entered for the reasons noted above and therefore the arguments directed to the amended claims are moot.

Thus, all rejections are maintained, for reasons of record.